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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/038,984	01/04/2002	Yin-Xiong Li	275.0003 0102	9705
26813 7590 12/22/2006 MUETING, RAASCH & GEBHARDT, P.A. P.O. BOX 581415 MINNEAPOLIS, MN 55458			EXAMINER VIVLEMORE, TRACY ANN	
			ART UNIT	PAPER NUMBER
			1635	
SHORTENED STATUTORY PERIOD OF RESPONSE		MAIL DATE	DELIVERY MODE	
3 MONTHS		12/22/2006	PAPER	

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No. 10/038,984	Applicant(s) LI ET AL.	
	Examiner Tracy Vivlemore	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 20 September 2006 and 16 October 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 75,76,78,79 and 82-98 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 75,76,78,79 and 82-98 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>9/20/06</u> . | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any rejection not reiterated in this Action is withdrawn.

Response to arguments: Claim Rejections - 35 USC § 102

Claims 75, 76, 78, 79, 82-91 and 93-98 are rejected under 35 U.S.C. 102(e) as being anticipated by Fire et al. (US 6,506,559, of record). This rejection is maintained for the reasons set forth in the office action mailed April 20, 2006.

In the remarks filed 10/16/06, applicants argue that Fire does not anticipate the claims as amended, asserting that at no point does Fire et al. disclose explanting a vertebrate cell from a vertebrate organism, supplying the cell with double stranded RNA to specifically attenuate expression of the target gene and implanting the cell into a vertebrate organism wherein expression of the target gene is attenuated.

These arguments are not persuasive because Fire discloses at column 6, lines 35-43 that the methods of the invention specifically attenuate gene expression by administration of double stranded RNA to a cell. At column 8 the method is disclosed as being performed in vertebrates. At column 10, lines 12-14 the invention is disclosed as including methods performed in cells *ex vivo* (explanted cells) and subsequently implanted into an organism. Therefore, the disclosure of Fire et al. does anticipate the claims as amended.

Applicants additionally argue that Fire himself expressed doubts about the applicability of this technology to vertebrates in a review published subsequent to the

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filing of the '559 patent. These remarks are noted, however a prior art reference is presumed to be operable in the absence of factual evidence to the contrary. Any opinions that might have been expressed by Fire do not change the contents of the '559 patent disclosure.

In the remarks filed 9/20/06, applicants argue that Fire et al. does not provide an enabling disclosure for vertebrate cells as set forth in instant claim 75, pointing out that all of the examples described in Fire were performed in *C. elegans*, a primitive invertebrate routinely grown on petri plates. Applicants conclude that description of dsRNA administration to this simple organism does not provide an enabling disclosure for the claimed methods in vertebrate cells. While it is correct that the working examples described in Fire are directed solely to invertebrates, a patent is prior art for all that it contains; it is not limited to a preferred or exemplified embodiment.

In the remarks filed 10/16/06 applicants additionally note that claims in a continuing application of the Fire patent have been rejected as non-enabled and, based on the existence of that rejection, argue that the Fire patent is not enabling prior art. These arguments are not persuasive because the Federal Circuit has made it clear that the level of enablement necessary for a reference applied under 102 is not identical to the enablement requirement applied to an application that is under examination. See for example the opinion issued November 20, 2006 in *IMPAX LABORATORIES, INC., v. AVENTIS PHARMACEUTICALS INC.*, CAFC docket number 05-1313:

"The enablement requirement for prior art to anticipate under section 102 does not require utility, unlike the enablement requirement for patents under section 112.9 *Rasmusson v. SmithKline Beecham Corp.*, 413 F.3d 1318, 1325-26 (Fed. Cir. 2005) ("[A] prior art reference need not demonstrate utility in order to serve as an anticipating reference under section 102." (citing *In re Schoenwald*, 964 F.2d 1122, 1124 (Fed. Cir. 1992); *In re Donohue*, 632 F.2d 123, 126 n.6 (C.C.P.A. 1980)); see also *In re Samour*, 571 F.2d 559, 563-64 (C.C.P.A. 1978); *In re Hafner*, 410 F.2d 1403, 1405 (C.C.P.A. 1969). In *Rasmusson*, we held that the Board of Patent Appeals and Interferences

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("Board") erred in determining that a prior art reference was not enabling and thus not anticipatory. 413 F.3d at 1325-26. The patent application in Rasmusson claimed a method of treating prostate cancer by using a chemical called finasteride. Id. at 1320. The prior art reference disclosed a method of treating prostate cancer by using finasteride, but the Board found that the prior art reference was not enabling because it failed to demonstrate that finasteride was "effective" in treating prostate cancer. Id. at 1325-26. We reversed the Board's determination that the prior art was not enabling and remanded the case for consideration of anticipation, holding that proof of efficacy is not required for a prior art reference to be enabling under section 102. Id.; see also Novo Nordisk Pharms., Inc. v. Bio-Tech. Gen. Corp., 424 F.3d 1347, 1355 (Fed. Cir. 2005) ("The standard for enablement of a prior art reference for purposes of anticipation under section 102 differs from the enablement standard under 35 U.S.C. § 112. . . . While section 112 'provides that the specification must enable one skilled in the art to "use" the invention,' . . . 'section 102 makes no such requirement as to an anticipatory disclosure,' Significantly, we have stated that 'anticipation does not require actual performance of suggestions in a disclosure. Rather, anticipation only requires that those suggestions be enabled to one of skill in the art.'" (citations omitted)); Bristol-Myers Squibb Co. v. Ben Venue Labs., Inc., 246 F.3d 1368, 1378 (Fed. Cir. 2001) (holding that prior art that suggested a drug was ineffective nevertheless anticipated a patent on that drug); Celeritas Techs. v. Rockwell Int'l Corp., 150 F.3d 1354, 1361 (Fed. Cir. 1998) ("A reference is no less anticipatory if, after disclosing the invention, the reference then disparages it. Thus, the question whether a reference 'teaches away' from the invention is inapplicable to an anticipation analysis.").

Claim Rejections - 35 USC § 103

Claims 75, 76, 78, 79 and 82-98 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al. (of record) in view of Ekenberg et al. (Promega Notes Magazine 1994).

The claimed invention is directed to methods of attenuating gene expression *ex vivo* in an explanted vertebrate cell by administration of double stranded RNA and implantation of the cell into an animal. In specific embodiments the cell is implanted into the same animal, the RNA is less than 200 base pairs, and the target gene is endogenous, foreign, chromosomal or from a pathogen. The double stranded RNA can be formed from one strand or two complementary strands and may be treated with RNase prior to delivery to a cell.

Fire et al. teach a method of inhibiting gene expression using double stranded RNA. Fire et al. teach that the method is general and target organisms include vertebrates such as fish. The genes targeted can be endogenous or a transgene, which is a foreign gene, or can be from a pathogen. The dsRNA can be formed from 1 or 2

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strands, the method can be used to treat disease and the dsRNAs can be delivered via several different means. At column 9 Fire et al. teach that the RNA can be purified before administration to a cell. Fire et al. do not teach the use of RNase to purify the double stranded RNA prior to administration.

It was well known in the art at the time of invention that RNases such as RNase A and RNase T specifically degrade single stranded RNA in the presence of double stranded RNA. See for example Ekenberg et al., who describe a protocol for RNase protection assays. This assay involves hybridization of an RNA probe and target, followed by removal of remaining single stranded RNA with an RNase specific for single stranded RNA in order to leave only RNA that is part of a double stranded structure.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use RNA purified by treatment with RNase in the method of inhibiting gene expression with double stranded RNAs taught by Fire et al. One of ordinary skill in the art would be motivated to purify the RNA used for inhibition of gene expression because Fire et al. specifically suggest use of purified RNA. One of ordinary skill would have been motivated to use an RNase specific for single stranded RNA for purification and would have had a reasonable expectation of success in doing so because the use of single-strand specific RNases in order to distinguish between single and double stranded RNA in RNase protection assays was well known.

Thus, the invention of claims 75, 76, 78, 79 and 82-98 would have been obvious, as a whole, at the time of invention.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Schultz, can be reached on 571-272-0763. The central FAX Number is 571-273-8300.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight

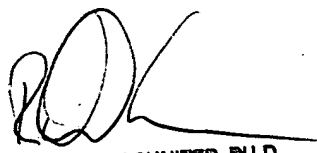
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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore
Examiner
Art Unit 1635

TV
December 15, 2006



RICHARD SCHNIZER, PH.D.
PRIMARY EXAMINER